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FILE 'HOME' ENTERED AT 12:58:03 ON 09 MAY 2003

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=> s (CPT-11 or irinotecan or camptostar)

L1 10060 (CPT-11 OR IRINOTECAN OR CAMPTOSTAR)

=> s (TRAIL or DR5 or Apo2)

L2 20664 (TRAIL OR DR5 OR APO2)

=> s l1 and l2

L3 34 L1 AND L2

=> dup rem l3

PROCESSING COMPLETED FOR L3

L4 17 DUP REM L3 (17 DUPLICATES REMOVED)

=> s l4 and py<=1999

2 FILES SEARCHED...

4 FILES SEARCHED...

L5 4 L4 AND PY<=1999

=> d ibib abs 1-4

L5 ANSWER 1 OF 4

MEDLINE

ACCESSION NUMBER:

2000090232

MEDLINE

DOCUMENT NUMBER:

20090232

PubMed ID: 10626806

TITLE:

Tumor necrosis factor-related apoptosis-inducing ligand's antitumor activity in vivo is enhanced by the chemotherapeutic agent CPT-11.

AUTHOR: Gliniak B; Le T
CORPORATE SOURCE: Department of Molecular Immunology, Immunex Corp., Seattle, Washington 98101, USA.. gliniak@immunex.com
SOURCE: CANCER RESEARCH, (1999 Dec 15) 59 (24) 6153-8.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000204
Last Updated on STN: 20000204
Entered Medline: 20000124

AB Tumor necrosis factor-related apoptosis-inducing ligand (**TRAIL**) can induce apoptosis in a wide variety of transformed human cells in vitro. In this study, the antitumor activity of recombinant **TRAIL** was analyzed in mice bearing human colon carcinoma tumors. We found that these tumors displayed a differential sensitivity to **TRAIL** in vivo that paralleled their susceptibility to **TRAIL**-induced apoptosis in vitro. Treatment of **TRAIL**-sensitive tumors 3 days after tumor challenge resulted in a dose-dependent inhibition of growth and the elimination of tumors in many mice. Colon carcinoma cell lines could be further sensitized to **TRAIL**-induced apoptosis in vitro by the addition of the chemotherapeutic agent camptothecin. Moreover, the combination of **TRAIL** and **CPT-11**, a water-soluble analogue of camptothecin, greatly enhanced the antitumor activity of **TRAIL** in vivo. **TRAIL** plus **CPT-11** treatment of both 3- and 10-day established **TRAIL**-sensitive tumors resulted in both a significant inhibition of tumor growth and a high proportion of complete tumor regressions. Treatment of **TRAIL**-resistant tumors with **TRAIL** and **CPT-11** dramatically slowed tumor growth and induced a transient tumor regression. These data demonstrate that **TRAIL** alone is a potent antitumor agent in vivo, and its activity can be significantly enhanced in combination with the chemotherapeutic agent **CPT-11**.

L5 ANSWER 2 OF 4 MEDLINE
ACCESSION NUMBER: 1999340100 MEDLINE
DOCUMENT NUMBER: 99340100 PubMed ID: 10411544
TITLE: Safety and antitumor activity of recombinant soluble Apo2 ligand.
AUTHOR: Ashkenazi A; Pai R C; Fong S; Leung S; Lawrence D A; Marsters S A; Blackie C; Chang L; McMurtrey A E; Hebert A; DeForge L; Koumenis I L; Lewis D; Harris L; Bussiere J; Koeppen H; Shahrokh Z; Schwall R H
CORPORATE SOURCE: Department of Molecular Oncology, Genentech Inc., 1 DNA Way, South San Francisco, CA 94080-4990, USA.
SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (1999 Jul) 104 (2) 155-62.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990820
Last Updated on STN: 19990820
Entered Medline: 19990812

AB TNF and Fas ligand induce apoptosis in tumor cells; however, their severe toxicity toward normal tissues hampers their application to cancer therapy. Apo2 ligand (Apo2L, or **TRAIL**) is a related molecule that triggers tumor cell apoptosis. Apo2L mRNA is expressed in many tissues, suggesting that the ligand may be nontoxic to normal cells. To investigate Apo2L's therapeutic potential, we generated in bacteria a

potently active soluble version of the native human protein. Several normal cell types were resistant in vitro to apoptosis induction by Apo2L. Repeated intravenous injections of Apo2L in nonhuman primates did not cause detectable toxicity to tissues and organs examined. Apo2L exerted cytostatic or cytotoxic effects in vitro on 32 of 39 cell lines from colon, lung, breast, kidney, brain, and skin cancer. Treatment of athymic mice with Apo2L shortly after tumor xenograft injection markedly reduced tumor incidence. Apo2L treatment of mice bearing solid tumors induced tumor cell apoptosis, suppressed tumor progression, and improved survival. Apo2L cooperated synergistically with the chemotherapeutic drugs 5-fluorouracil or CPT-11, causing substantial tumor regression or complete tumor ablation. Thus, Apo2L may have potent anticancer activity without significant toxicity toward normal tissues.

L5 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 ACCESSION NUMBER: 1994:486525 BIOSIS
 DOCUMENT NUMBER: PREV199497499525
 TITLE: 7-Ethyl-10-(4-(1-piperidino)-1-piperidino) carbonyloxy camptothecin: Mechanism of resistance and clinical trails.
 AUTHOR(S): Saijo, Nagahiro (1); Nishio, Kazuto; Kubata, Naohiro; Kanzawa, Fumihiko; Shinkai, Tetsu; Karato, Atsuya; Sasaki, Yasutsuna; Eguchi, Kenji; Tamura, Tomohide; et al.
 CORPORATE SOURCE: (1) Pharmacol. Div., Natl. Cancer Cent. Res. Inst., Tsukiji 5-1-1, Chuo-ku, Tokyo 104 Japan
 SOURCE: Cancer Chemotherapy and Pharmacology, (1994) Vol. 34, No. SUPPL., pp. S112-S117.
 ISSN: 0344-5704.
 DOCUMENT TYPE: Article
 LANGUAGE: English

AB The camptothecin derivative 7-ethyl-10-(4-(1-piperidino)-1-piperidino)-carbonyloxy camptothecin (CPT-11) has attracted the attention of clinicians because of its high antitumor activity against refractory solid cancers. We established two CPT-11-resistant cell lines, a non-small-cell lung-cancer cell line (PC-7/CPT-11) from the parental PC-7 line and an ovarian cancer cell line (HAC-2/CPT-11) from the parental HAC-2 line. The mechanisms of resistance to CPT-11 in PC-7/CPT-11 cells were reduced conversion of CPT-11 to its active metabolite SN-38 and point mutation of topoisomerase I. Those in HAC-2/CPT-11 cells were reduction of topoisomerase I activity and decreased sensitivity of topoisomerase to topoisomerase I inhibitors. No point mutation of the topoisomerase was observed in HAC-2/CPT-11 cells. We conducted two phase I trials using CPT-11 in combination with other anticancer agents. One was a phase I trial of CPT-11 and cisplatin given with a fixed dose of vindesine to patients with advanced non-small-cell lung-cancer and the other was a phase I study on a topoisomerase-targeting combination of CPT-11 and etoposide (VP-16) in patients with various malignant solid tumors. The results of the first trial indicated that the recommended dose of CPT-11 for phase II studies was 80 mg/m-2 combined with 3 mg/m-2 vindesine on days 1 and 8 and 60 mg/m-2 cisplatin on day 1. In the second trial, the recommended dose of CPT-11/VP-16 given with recombinant granulocyte colony-stimulating factor (on days 4-17) was found to be 60/60 mg/m-2. In both trials, diarrhea and granulocytopenia were considered to be dose-limiting toxicities.

L5 ANSWER 4 OF 4 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
 ACCESSION NUMBER: 1999247940 EMBASE
 TITLE: Prognostic factors of non-small cell lung cancer patients with malignant pleural effusion.
 AUTHOR: Seto T.; Semba H.; Seto M.; Nishida Y.; Fukai Y.

CORPORATE SOURCE: T. Seto, Division of Respiratory Diseases, Kumamoto
Regional Medical Center, Kumamoto, Japan
SOURCE: Japanese Journal of Lung Cancer, (1999) 39/3 (303-308).
Refs: 12
ISSN: 0386-9628 CODEN: HGANAO
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
037 Drug Literature Index
LANGUAGE: Japanese
SUMMARY LANGUAGE: English; Japanese

AB Prognostic factors in 70 patients with non-small cell lung cancer (NSCLC) with malignant pleural effusion at initial treatment were examined retrospectively. They constituted 11% of the patients with NSCLC, diagnosed at our hospital from 1990 to 1997. Although 9 of the patients had negative in effusion cytology findings, malignant effusion was diagnosed by thorascopic pleural biopsy under local anesthesia. Of the patients with malignant pleural effusion 89% were adenocarcinoma of the lung. Using non-parametorical method analyses, N-factor ($p=0.0105$), clinical stage (0.0247), ECOG performance status (0.001), protein value of effusion (0.0095), and effusion volume/day (0.0019) were recognized as prognostic factors. Furthermore, N-factor and low protein value of effusion were poor predictive factors for survival, and intra-pleural chemotherapy and systemic chemotherapy were related to good survival in multivariate analysis. In clinical **trial** for patients with malignant pleural effusion, we must carefully compare these pre-treatment factors.

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NEWS	3	Jun 03	New e-mail delivery for search results now available
NEWS	4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS	5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS	6	Aug 26	Sequence searching in REGISTRY enhanced
NEWS	7	Sep 03	JAPIO has been reloaded and enhanced
NEWS	8	Sep 16	Experimental properties added to the REGISTRY file
NEWS	9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS	10	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS	11	Oct 24	BEILSTEIN adds new search fields
NEWS	12	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS	13	Nov 18	DKILIT has been renamed APOLLIT
NEWS	14	Nov 25	More calculated properties added to REGISTRY
NEWS	15	Dec 04	CSA files on STN
NEWS	16	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS	17	Dec 17	TOXCENTER enhanced with additional content
NEWS	18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS	19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS	20	Feb 13	CANCERLIT is no longer being updated
NEWS	21	Feb 24	METADEX enhancements
NEWS	22	Feb 24	PCTGEN now available on STN
NEWS	23	Feb 24	TEMA now available on STN
NEWS	24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS	25	Feb 26	PCTFULL now contains images
NEWS	26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS	27	Mar 19	APOLLIT offering free connect time in April 2003
NEWS	28	Mar 20	EVENTLINE will be removed from STN
NEWS	29	Mar 24	PATDPAFULL now available on STN
NEWS	30	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS	31	Apr 11	Display formats in DGENE enhanced
NEWS	32	Apr 14	MEDLINE Reload
NEWS	33	Apr 17	Polymer searching in REGISTRY enhanced
NEWS	34	Apr 21	Indexing from 1947 to 1956 being added to records in CA/CAPLUS
NEWS	35	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS	36	Apr 28	RDISCLOSURE now available on STN
NEWS	37	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS EXPRESS			April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
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NEWS INTER			General Internet Information